Remarks

Sequence Requirements

The specification is in the process of being reviewed and amendments will be provided as appropriate.

Double Patenting

Since the examiner has made of record the equivalence of claims 26-33 and 59-66, claims 59-66 have been cancelled.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 26-34 and 59-67 were rejected under 35 U.S.C. § 112, first paragraph, as not being enabled. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Since the majority of the examiner's argument appears to relate to the issue of infection and appropriate animals models, the preamble of the claims has been amended to refer to "prevention of viral budding" rather than "viral infection". One does not have to have an animal model to study viral budding (although most virologists also know that only cell culture, not animal models, are required to study infection).

The Legal Standard for Enablement

The Court of Appeals for the Federal Circuit (CAFC) has described the legal standard for enablement under § 112, first paragraph, as whether one skilled in the art could make and use the claimed invention from the disclosures in the patent coupled with information known in the art, without undue experimentation (*See, e.g., Genentech, Inc. v. Novo Nordisk A/S*, 108 F3d at 165,

42 USPQ2d at 1004 (quoting *In re Wright*, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); See also *In re Fisher*, 427 F.2d at 839, 166 USPQ at 24; *United States v. Telectronics, Inc.*, 857 F.2d 778 (Fed. Cir. 1988); *In re Stephens*, 529 F.2d 1343 (CCPA 1976)). The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation (*M.I.T. v. A.B. Fortia*, 774 F.2d 1104 (Fed. Cir. 1985)). In addition, as affirmed by the Court in *Spectra-Physics, Inc. v. Coherent, Inc.*, 827 F.2d 1524 (Fed. Cir. 1987), a patent need not teach, and preferably omits, what is well known in the art.

Whether the disclosure is enabling is a legal conclusion based upon several underlying factual inquiries. See *In re Wands*, 858 F.2d 731, 735, 736-737, 8 USPQ2d 1400, 1402, 1404 (Fed. Cir. 1988). As set forth in *Wands*, the factors to be considered in determining whether a claimed invention is enabled throughout its scope without undue experimentation include the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims. In cases that involve unpredictable factors, "the scope of the enablement obviously varies inversely with the degree of unpredictability of the factors involved." *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The fact that some experimentation is necessary does not preclude enablement; what is required is that the amount of experimentation 'must not be unduly extensive.' *Atlas Powder Co., v. E.I. DuPont De Nemours*

& Co., 750 F.2d 1569, 1576, 224 USPQ 409, 413 (Fed. Cir. 1984). There is no requirement for examples.

The claims are directed to inhibiting/preventing virus budding *via* a Phospholipid Scramblase polypeptide or fragment thereof. The examiner asserts that the results of Example 4 are ambiguous for whether the cytokine or the enzyme had a direct effect on VSV replication. The applicants readily admit that IFN is known to inhibit VSV at different stages in its life cycle by different anti-viral pathways. The results in Example 4 indicate that the phospholipid scramblase ***cooperates*** with other IFN-induced proteins in the inhibition of VSV replication (see paragraph 0139). However, as shown in the preceding paragraph (0138) and previously stated by the applicants, the viability of phospholipid scramblase cDNA expressing cells was 33% (compared to that of vector control cells: 7%). The assay was conducted using VSV stably transfected HEY 1B cells. "Therefore, expression of PLSCR1 resulted in a significant reduction in the cytopathic effect of VSV infection" (see last sentence of paragraph 0138; wherein no cytokine was present). At an MOI of 10 pfu (10 plaque forming units roughly equal to 10 viruses per cell), a 26% increase in viable cells ***is statistically significant*** (33% - 7% = 26%). The results of Example 4 clearly show an inhibition, or regression, of the disease state of the transfected cell line. This is clearly sufficient to support claims to a method of prevention of viral budding. Example 4 clearly shows that there was no adverse effect on routine cellular function (addressing examiners concern of page 7, first paragraph, of the office action mailed on February 25, 2003).

The presence of the claimed motif enables inhibition of viral budding. Given the technology at the time of filing the present application, one of ordinary skill in the art would be able to synthesize and/or isolate polypeptides having such activity. Furthermore, the targeted protein domain is well characterized (WW domain). Therefore, the structural features common to the claimed PPxY containing scramblases, also defined by the WW domain and the complementary forces it contains for proper binding by the PPxY domain (for example, the requisite hydrogen bonding acceptor and donor sites, electrostatic interactions, and geometric and steric constraints of the WW domain), are known and readily discernable and available to those skilled in the art.

In summary, the legal test is not whether or not there are embodiments that the person of skill in the art may not be able to practice or that may not meet FDA requirements. The test is only whether one of skill in the art can practice that which is claimed, to some degree, without undue experimentation, and with a reasonable expectation of success. Applicants have clearly met this requirement.

Allowance of claims 26-34 is respectfully solicited.

Respectfully submitted,

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Certificate of Facsimile Transmission

I hereby certify that this Amendment and Response to Office Action, and any documents referred to as attached therein are being facsimile transmitted on this date, March 1, 2004, to the Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450.

Jean Hicks

Date: March 1, 2004

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